

large expanses of the cytoplasm contain no elements of the network” (1958a, p. 289).<sup>31</sup> If the particles could exist independently of the endoplasmic membrane, what was the significance of their association with the membrane in many adult cells? Palade speculated,

it may be assumed that the reticulum provides appropriate surface for the arrangement of the small granules, but thus far we do not know whether the patterns described have any significant role in protein synthesis. Available information suggests, however, other possible reasons. In certain cells, for instance, the cavities of the endoplasmic reticulum appear to be in continuity, at least intermittently, with the extracellular medium through invaginations of the cell membrane. In such cases the supposedly fluid phase that occupies the cavities of the network may contain a variable amount of the extracellular fluid. It is possible that many raw materials, coming from outside into the cytoplasm, reach the particles through the labyrinth of the endoplasmic reticulum. In other cells the cavities of the endoplasmic reticulum appear to be used for the storage of a cell product. In plasma cells, thyroid epithelia, and fibroblasts they are frequently found distended and filled with an apparently amorphous mass of appreciable density. There are, in other words, numerous appearances suggesting that the cavities of the reticulum serve as feeding channels and storage space for the activity of the particles. Their association may have the same significance as the location of our plants along convenient ways of communication. (p. 301)

From the perspective of developing a model of a mechanism, Palade has here offered a decomposition into distinct operations: supplying materials, synthesizing proteins, and transporting the products. Palade (1958b) further developed this perspective, drawing insights from the nineteenth-century research of Rudolf Peter Heinrich Heidenhain (1875), who had found that in exocrine cells of the pancreas, granules disappear after food intake and are replaced with new granules a few hours later. Heidenhain concluded that the granules were comprised of the precursors of the digestive enzymes of pancreatic juice and that they provided temporary storage for these proteolytic enzymes. He named them zymogen granules. Following up on Heidenhain’s research, Siekevitz and Palade compared the appearance of the endoplasmic reticulum in cells from guinea pigs starved for forty-eight hours with cells from guinea pigs fed an hour before. In the recently fed animals, “the cavities

<sup>31</sup> A note indicates that the text of this paper was prepared for a talk in February 1955, and was largely unaltered until publication. Palade commented on the rather unusual patterns of the particles on the endoplasmic reticulum membrane: “Sometimes, while looking at these intriguing patterns, I believe that I feel very much like the French explorers who, during Napoleon’s expedition to Egypt, found themselves face to face with the hieroglyphs. Like some of them, I am recording the patterns, and I am waiting hopefully for a biochemical Champollion to decipher their meaning.”